Remarks

Claims 1 to 15 are pending in the instant application. Claims 1 and 6, as well as withdrawn Claims 11-14 are amended, and Claims 2-5, 8-10 and 15 are cancelled herein. With entry of these amendments Claims 1, 6 and 7 directed to multivalent bleb preparations and vaccines including the multivalent bleb preparations are under consideration. In the event that Claims 1, 6 and/or 7 are found to be allowable, Applicants respectfully request rejoinder of the withdrawn process Claims 11-14 that are dependent from and incorporate all of the limitations the product claims.

No new matter is added by way of the amendments to the claims. Support for the amendments to the claims is found, for example, in the claims as originally filed, as well as in the specification, including the Examples.

Examiner Interview

Applicants thank the Examiner for the Telephonic Interview with Applicants' undersigned attorney on 24 October 2007. Although no agreement was reached, Applicants appreciate the opportunity to discuss aspects of the claims and prior art.

Preliminary Remarks

As a preliminary matter, Applicants wish to clarify the previously stated position with respect to Berthet. As stated in the response submitted 15 February 2007 to the Office Action dated 28 November 2006, Applicants maintain that p. 35, lines 20-30, of Berthet, cited by the Examiner, relates specifically to characterizing "bleb preparations that are immunoprotective against a set of heterologous strans..." That is, the passage cited by the Examiner provides a definition of immunoprotection, and provides a list of strains to which protection should be conferred by a vaccine composition designed to protect against meningococcal infections. Applicants also maintain that p. 36, beginning with heading "Vaccine Combinations" on line 5, concerns multivalent bleb preparations, but does not expressly teach that "the different bleb preparations are selected such that at least one of the bleb preparations is deficient in PorA and that at least one other bleb preparation is not deficient in PorA." Applicants thank

the Examiner for drawing their attention to page 11 of the instant specification, which states that "particular multivalent bleb preparations disclosed in WO 01/09350 (such as a combination consisting of blebs derived from all of the following menB strains: H44/76, M97/252078, BZ10, NGP165 and CU385, or combinations consisting of blebs from CU385 and one or more bleb preparations derived from one or more of the other 4 strains) are not claimed." Additionally, Applicants recognize that because strain CU385 is PorA deficient and strain H44/76 is not deficient in PorA, that a combination of blebs derived from strain CU385 and strain H4475 would inherently possess the property of a combination of blebs one of which is PorA deficient, and one of which is not deficient in PorA. This inconsistency arose inadvertently and without deceptive intent. Applicants apologize to the Examiner for any confusion or inconvenience caused by this inadvertent oversight, and herein amend the claims accordingly.

Claims 1 and 6 (as amended) are directed to a "multivalent meningococcal bleb composition comprising a first bleb preparation deficient in PorA derived from the *Neisseria meningitidis* B CU-385 (B:4:P1.19,15 or "P1.15") strain and a second bleb preparation that is not deficient in PorA derived from a *Neisseria meningitidis* B:4:P1.7,b,4 ("P1.4") strain prevalent in New Zealand." Amended Claim 7 is directed to a vaccine composition for protecting against meningococcal disease that contains the multivalent bleb compositions. Applicants believe that the claimed composition offers particularly beneficial cross-protection against multiple strains of *Neisseria meningitidis* circulating in populations, *e.g.*, in New Zealand. The recognition by the inventors that combinations of blebs that include at least a first bleb preparation deficient in PorA and at least a second bleb preparation that is not deficient in PorA provide superior immune responses to heterologous strains, and offer benefits in production over vaccines made with the many different blebs that would be necessary to provide adequate protection against strains of the various heterologous serosubtypes. Specifically, the CU-385 strain has been identified as a particularly suitable strain for vaccine preparation, (for example, when combined with B:4:P1.7,b,4 strain prevalent in New Zealand) has been shown to be particularly effective in the context of a multivalent bleb vaccine for protecting against meningococcal disease caused by strains of different serosubtypes due to the relative deficiency in PorA expression by CU-385. Such a

composition is particularly advantageous in the context of a vaccine because it minimizes the number of blebs necessary to provide specific, as well as cross-protection, thus facilitating vaccine production and minimizing vaccine cost. In view of the foregoing, Applicants respectfully request reconsideration of the claims.

Claims Rejections Under 35 U.S.C. § 102 and 103

Claims 1, 6 and 7 are novel

Claims 1 to 9 and 15 stand rejected under 35 USC 102 (b) as being anticipated by Berthet, *et al.* (WO 01/09350; "Berthet") and also by Granoff, *et al.* (WO 02/09643; "Granoff").. To the extent that the Examiner maintains the rejection with respect to amended Claims 1, 6 and 7, Applicants traverse and respectfully request reconsideration of the claims in view of the following remarks.

Under U.S. patent law "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Thus, in order for either Berthet or Granoff, to anticipate Claims 1, 6 and 7 of the instant application, the cited reference must expressly or inherently disclose a multivalent meningococcal bleb composition comprising a first bleb preparation deficient in PorA derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA derived from a *Neisseria meningitidis* B:4:P1.7,b,4 strain prevalent in New Zealand.

Although Berthet expressly discloses the CU-385 strain, Berthet does not expressly disclose the B:4:P1.7,b,4 strain prevalent in New Zealand. Since, strains of this sero and subtype are not inherent in any of the other strains disclosed by Berthet, this reference does not inherently disclose a strain of the B:4:P1.7,b,4 strain prevalent in New Zealand. Accordingly, Berthet does not expressly or inherently disclose all of the limitations of the claims and cannot anticipate Claims 1, 6 and 7. Accordingly, the rejection of Claims 1, 6 and 7 as anticipated by Berthet under 35 U.S.C. 102(b) should be withdrawn.

Granoff relates to immunization with blebs of three specific strains, RM1090, BZ198 and Z1092, each of which is selected from a different serotype. That is, RM1090 is a *N. meningitidis* C strain (C:2a:P1.5,2:L3,7); BZ198 is a *N. meningitidis* B strain (B:NT:P1.4); and Z1092 is a *N. meningitidis* A strain (A:4,21:P1.10). Granoff teaches that sequential administration of such compositions is preferred to administration of a mixture. None of the strains administered by Granoff is CU-385, and none of the strains is a *Neisseria meningitidis* B:4:P1.7,b,4 strain prevalent in New Zealand. Reference to CU-385 is only made with respect to its use in an experimental model to test bactericidal activity of sera generated against other strains of meningococcus, and Applicants are aware of no mention by Granoff of any *Neisseria meningitidis* B:4:P1.7,b,4 strain. Accordingly, Granoff does not teach all of the elements of amended Claims 1, 6 and 7, and the rejection over Granoff *et al.* under 102(b) should be withdrawn.

Claims 1, 6 and 7 are non obvious

Claims 1-9 and 15 also stand rejected under 35 U.S.C. 103(a) as allegedly rendered obvious by Berthet in view of Lehmann *et al.* APMIS 99:769-772, 1991; "Lehmann") and/or Granoff. To the extent that the Examiner maintains these rejections with respect to amended Claims 1, 6 and 7, Applicants traverse, and request reconsideration in view of the following remarks.

Under 35 U.S.C. § 103, a patent may not be obtained if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103. In view of the Supreme Court's recent decision in *KSR Int'l v. Teleflex Inc.*, the Examiner is required "to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." Memorandum to Technology Center Directors on the subject of the Supreme Court decision on *KSR Int'l Co., v. Teleflex, Inc.,* dated May 03, 2007. A proper rejection under 35 USC § 103 requires that the Examiner 1) identify prior art that differs from the claimed subject matter only in a way that would have been obvious at the time the invention was made, and 2) to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.

The Examiner states (page 9 of the Office Action) that: "it is clear from reading Berthet, that vaccines containing blebs from multiple strains are disclosed; and that strains CU-385 and H44/76 have been contemplated. Moreover, applicant explicitly recognized tha Berthet discloses combinations of blebs from strains H44/76 and CU-385 on page 11, lines 29-33 of the instant specification." The Examiner alleges (page 10 of the Office Action) that Lehmann "disclose an outer membrane vesicle (bleb) vaccine comprising blebs from a meningococcal strain with the serosubtype P1.16. The Examiner contends that "it would have been obvious to one of ordinary skill in the art to use blebs from a meningococcal strain with the serosubtype P1.16 in the vaccine composition of Berthet *et al.*" because the two compositions are used for the same purpose.

However, subject Claims 1, 6 and 7 relate specifically to multivalent bleb preparations that include CU-385 and a second bleb preparation that is not deficient in PorA derived from a *Neisseria meningitidis* B:4:P1.7,b,4 strain prevalent in New Zealand. This second strain is not H44/76 (P1.7,16) and is not a meningococcal strain with the serosubtype P1.16. Thus, the teaching in Lehmann of a vaccine containing a meningococcal strain with the serosubtype P1.16 does supply any element missing from Berthet. Accordingly, combining the teachings would still not teach all of the limitations of the compositions of Claims 1, 6 and 7, and cannot render these claims obvious. Therefore, Applicants respectfully request that the rejection be withdrawn.

As discussed above, Granoff concerns administration (preferably sequentially) of blebs derived from *Neisseria meningitidis* serotypes A, B and C, and does not teach compositions that include a first bleb preparation deficient in PorA derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA derived from a *Neisseria meningitidis* B:4:P1.7,b,4 strain prevalent in New Zealand. Since the Examiner has provided no explanation of why or how one of skill in the art would have combined or modified the prior art elements in the manner of Claims 1, 6 an 7, Applicants respectfully request that the rejection be withdrawn.

Conclusion

On the basis of the amendments and remarks above, Applicants believe that the claims are now in condition for allowance. If the Examiner believes that a telephonic interview would expedite prosecution and/or clarify or simplify any of the issues under consideration, the Examiner is invited to contact the undersigned to arrange for an Examiner's interview, or to discuss the status of this application.

Respectfully submitted,

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